-- 36. A method for monitoring denaturation of a protein at a specific site in vivo during interventional therapy comprising the steps of:

(a) administering to a human or animal patient a contrast agent comprising a physiologically compatible, chelated paramagnetic metal ion wherein the contrast agent has an affinity for a protein in its native state within a diseased tissue of the patient;

(b) executing an interventional therapy selected from the group consisting of

(1) application of a focused external energy source capable of causing denaturation of said protein within said diseased tissue; and

(2) injection of a chemical compound or composition directly into said diseased tissue wherein said chemical compound or composition is capable of causing denaturation of said protein within said diseased tissue;

(c) contemporaneously executing said interventional therapy and magnetic resonance imaging of said diseased tissue;

(d) determining the extent of protein denaturation by monitoring the extent to which the contrast agent remains bound to said protein during said interventional therapy;

(e) discontinuing said interventional therapy if either the therapy is complete or if the denaturation of said protein is unacceptably high; and

(f) repeating any of the above steps.

37. A method for monitoring viability of a tissue

using MRI comprising the steps of:

(a) administering to a human or animal patient that is undergoing interventional therapy a contrast agent comprising a physiologically compatible, chelated paramagnetic metal ion and binding moiety that has a higher affinity for the tissue in its native state than it has for the tissue in a degraded state;

(b) monitoring the viability of the tissue at the site of the interventional therapy by measuring the change in signal intensity during the interventional therapy and imaging of said diseased tissue;

(c) discontinuing said interventional therapy if either the therapy is complete or if the degradation of said protein is unacceptably high; and

(d) repeating any of the above steps.

38. The method of claim 36 or 37, wherein the physiologically compatible, chelated paramagnetic metal ion has as its chelate DTPA, DOTA, DTPA-BMA, or HP-DO3A.

39. The method of claim 36 or 37, wherein the physiologically compatible, chelated paramagnetic metal ion is selected from the group having atomic numbers 13, 21-34, 39-42, 44-50 and 57-83.

40. The method of claim 39, wherein the physiologically compatible, chelated paramagnetic metal ion is selected from the group having atomic numbers 21-29, 42, 44 and 57-83.

41. The method of claim 40, wherein the physiologically compatible, chelated paramagnetic metal ion is selected from the group consisting of Gd(III), Fe(III), Mn(II), Mn(III), Cr(III), Cu(II), Dy(III), Tb(III), Ho(III), Er(III) and Eu(III).

42. The method of claim 41, wherein the metal ion is Gd(III).

43. The method of claim 36 or 37, wherein said protein in its native state is a component of plasma, interstitial space, synovial fluid, cerebral spinal fluid, inflammatory fluid, abcess fluid or intracellular space.

44. The method of claim 36 or 37, wherein said protein is selected from the group consisting of human serum albumin, fatty acid binding protein, glutathione-S-transferase and lipoproteins.

45. The method of claim 44, wherein said protein is human serum albumin and at least 10% of the agent binds to the protein in its native state.

46. The method of claim 45, wherein at least 50% of the agent binds to human serum albumin in its native state.

47. The method of claim 46, wherein at least 80% of the agent binds to human serum albumin in its native state.

48. The method of claim 47, wherein at least 95% of the agent binds to human serum albumin in its native state.

49. The method of claim 44, wherein the contrast agent exhibits a binding affinity for said protein in its denatured state which is less than about 80% of the contrast agent's binding affinity for said protein in its native state.

50. The method of claim 44, wherein the contrast agent exhibits a binding affinity for said protein in its denatured state which is less than about 50% of the contrast agent's binding affinity for said protein in its native state.

51. The method of claim 44, wherein the contrast agent exhibits a binding affinity for said protein in its denatured state which is less than about 20% of the contrast agent's binding affinity for said protein in its native state.

52. The method of claim 44, wherein the contrast agent exhibits a binding affinity for said protein in its denatured state which is less than about 10% of the contrast agent's binding affinity for said protein in its native state.

53. The method of claims 36 or 37, wherein the contrast agent exhibits an R_1 relaxivity when bound to the tissue or tissue component in its denatured state which is less than about 80% of the R_1 relaxivity of the contrast agent when bound to the tissue or tissue component in its native state.

54. The method of claims 36 or 37, wherein the contrast agent exhibits an R_1 relaxivity when bound to the tissue or tissue component in its denatured state which is

less than about 50% of the R_1 relaxivity of the contrast agent when bound to the tissue or tissue component in its native state.

55. The method of claims 36 or 37, wherein the contrast agent exhibits an R_1 relaxivity when bound to the tissue or tissue component in its denatured state which is less than about 20% of the R_1 relaxivity of the contrast agent when bound to the tissue or tissue component in its native state.

56. The method of claims 36 or 37, wherein the contrast agent exhibits an R_1 relaxivity when bound to the tissue or tissue component in its denatured state which is less than about 10% of the R_1 relaxivity of the contrast agent when bound to the tissue or tissue component in its native state.

57. The method of claims 36 or 37, wherein the contrast agent exhibits an R_1 relaxivity when the interventional therapy is complete and the targeted tissue or tissue component is returned to physiological conditions which is less than about 80% of the R_1 relaxivity of the contrast agent when bound to the tissue or tissue component in its native state.

58. The method of claims 36 or 37, wherein the contrast agent exhibits an R_1 relaxivity when the interventional therapy is complete and the targeted tissue or tissue component is returned to physiological conditions which is less than about 50% of the R_1 relaxivity of the contrast agent when bound to the tissue or tissue component in its native state.

59. The method of claims 36 or 37, wherein the contrast agent exhibits an R_1 relaxivity when the interventional therapy is complete and the targeted tissue or tissue component is returned to physiological conditions which is less than about 20% of the R_1 relaxivity of the contrast agent when bound to the tissue or tissue component in its native state.

60. The method of claims 36 or 37, wherein the contrast agent exhibits an R_1 relaxivity when the interventional therapy is complete and the targeted tissue or tissue component is returned to physiological conditions which is less than about 10% of the R_1 relaxivity of the contrast agent when bound to the tissue or tissue component in its native state.

61. The method of claim 36 or 37, wherein the interventional therapy and imaging are both conducted while the contrast agent in present in the patient's body.

62. The method of claim 36 or 37, wherein the interventional therapy and imaging are contemporaneous.

63. The method according to claim 36 or 37, wherein the focused energy source is ultrasound or laser light. --

REMARKS

Applicants have canceled all previous claims following the Final Action of August 13, 1999 and the Notice of Appeal filed February 10, 2000. Claims 36-63 are now pending. Applicants assert that the amended claims obviate all rejections encountered previously during prosecution.

As a general point, Applicants would like to note